REMARKS

The Office Action mailed on November 13, 2000 (Paper No. 5) presented claim rejections for (1) new matter (35 U.S.C. §112, first paragraph); (2) enablement (35 U.S.C. §112, first paragraph); and (3) anticipation (35 U.S.C. §102(b)). Each of these issues is addressed below.

I. New Matter

Claims 21-42 of the parent application were rejected under 35 U.S.C. §112, first paragraph, because they allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

However, the claims above set forth methods for concurrently generating a secondary amplification product and an amplification product in a primer based nucleic acid amplification reaction. Such primer based nucleic acid amplification reactions that are the foundation for the claimed methods are not new matter to the present application.

There are numerous disclosures in the present application, as filed, that provide evidence that the inventors had possession of the claimed invention. Examples of such disclosures are set forth below with emphasis added.

> (1) The present invention is described generically as "a primer-based amplification detection method in which the need for a second amplification reaction is eliminated. (Column 3, lines 50-52).
>
> (2) Similarly, the originally filed specification generically defines an amplification primer as "a primer for amplification of a target sequence by primer extension." (Column 4, lines 1-2). The genericness of this description is confirmed by the next sentence that exemplifies a SDA amplification primer by further characterization as a species of the generic amplification primer.

(3) Extension products are also defined generically as "nucleic acids which comprise a primer and a newly synthesized strand which is the complement of the target sequence downstream of the primer binding site." (Column 4, lines 28-31). This definition also continues to generically state that "[e]xtension products result from hybridization of a primer to a target sequence and extension of the primer by polymerase using the target sequence as a template." (Column 4, lines 31-33).

(4) The terms target or target sequence are defined generically as "produced in the amplification reaction" referring back to the disclosed primer based amplification reaction. (Column 4, lines 46-52).

(5) The amplification products are similarly generically defined, and are specified as "including intermediates of the amplification reaction", again referring back to the disclosed primer based amplification reaction. (Column 4, line 63 - Column 5, line 2).

(6) In the discussion of methods for detection of a signal primer, it is noted that "[a]ll of these methods are useful in the present invention and one skilled in the art can routinely select appropriate methods for use in any particular amplification assay system". (Column 6, lines 21-24).

Thus, the application as filed provided a specification that conveys to one skilled in the relevant art that the inventors had possession of a method for concurrently generating a secondary amplification product and an amplification product in a primer based nucleic acid amplification reaction. Strand Displacement Amplification is a primer based nucleic acid amplification reaction that was disclosed with more particularly to exemplify the generic description provided in the specification.

It is therefore respectfully submitted that the claiming of such methods using a primer based nucleic acid amplification reaction does not constitute the addition of new matter to the application.

II. Enablement

Claims 21-42 of the parent application were also rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record.

In support of this rejection, it is stated that the Applicants' arguments in the previous response (filed September 22, 1999) take warnings in the specification out of context. It is also asserted the Applicants' discussion regarding the fact that undesirable high levels of background signal are not manifest in a primer based amplification method is not the issue.

However, it is respectfully submitted the Applicants' arguments do not take warnings in the specification out of context, and that Applicants' discussion of background signal levels was presented as the issue relating to enablement in the Office Action (Paper No. 2) to which the previous response was filed. Specifically, the issue of signal primers acting as amplification primers and thus creating undesirable high levels of background signal, was presented as support for the enablement rejection in Paper No. 2.

The Applicants merely responded to the asserted basis for the rejection by explaining why the claimed methods, using primer based nucleic acid amplification reactions as a foundation, would not cause the undesirable high levels of background signal as asserted in Paper No. 2. Specifically, Applicants explained that in practicing the claimed methods:

> any undesirable level of background signal will only be present upon the simultaneous mispriming of both the amplification primer and the signal primer. Even if such a simultaneous dual mispriming event occurs, the labeled signal primer (the only component capable of contributing to background signal) will only be a part of a linear extension reaction, which should not product background signal at a level comparable to the desired target signal.

The Applicants then showed the support for this technical explanation in the specification.

As noted in the original specification, "[h]igh levels of background signal are believed to be due to non-specific priming and subsequent amplification of spuriously primed non-target DNA" (emphasis added). (Column 6, lines 33-36). Also, as noted in the original specification, a single mispriming event "is comparatively rare", and thus "is detectable only after subsequent amplification of the misprimed sequence" (emphasis added). (Column 3, lines 57-59). Therefore, the simultaneous dual mispriming of an amplification primer and a signal primer downstream therefrom necessary for the displacement and linear extension of misprimed signal primer product will be an extremely rare occurrence. Furthermore, the original specification allows for some linear accumulation of signal primer product. (Column 5, lines 10-14).

Thus, the Applicants have addressed the sole basis for the enablement rejection by showing how the specification teaches the technological explanation for the foundation of the claimed methods. Furthermore, the explanations provided are not inconsistent with the alleged warnings of the specification, and therefore do not present such warnings out of context.

III. Anticipation

Claims 43-50 were rejected under 35 U.S.C. §102(b) as being anticipated by Mullis et al. (U.S. Patent No. 4,683,195) or Urdea (U.S. Patent No. 5,200,314).

However, claims 43-50 have been cancelled.

IV. Conclusion

The claims of the application are now believed to be in condition for allowance, and early notice thereof is respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please amend claims 21 and 29 as follows:

21. (amended) A method for concurrently generating a secondary amplification product and an amplification product in a primer based nucleic acid amplification reaction, the method comprising:

a) hybridizing a signal primer to a target sequence and hybridizing a first amplification primer to the target sequence upstream of the signal primer;

b) extending the hybridized signal primer on the target sequence to produce a signal primer extension product and extending the hybridized first amplification primer on the target sequence such that extension of the first amplification primer displaces the signal primer extension product from the target sequence;

c) hybridizing a second amplification primer to the signal primer extension product and extending the hybridized second amplification primer on the signal primer extension product to produce a second amplification primer extension product comprising a newly synthesized strand;

d) displacing the newly synthesized strand from the signal primer extension product; and

e) hybridizing the signal primer to the displaced newly synthesized strand and extending the signal primer such that a double stranded secondary amplification product is generated.

29. (amended) A method for concurrently generating a secondary amplification product and an amplification product in a primer based nucleic acid amplification reaction, the method comprising:

a) hybridizing a first signal primer to a first strand of a double-stranded target sequence and hybridizing a first amplification primer to the first strand of the target sequence upstream of the first signal primer;

b) extending the hybridized first signal primer on the first strand to produce a first extension product and extending the hybridized first amplification primer on the first strand such that extension of the first amplification primer displaces the first extension product from the target sequence;

c) hybridizing a second signal primer to the first extension product and hybridizing a second amplification primer to the first extension product upstream of the second signal primer;

d) extending the hybridized second signal primer on the first extension product to produce a second extension product and extending the hybridized second amplification primer on the first extension product such that extension of the second amplification primer displaces the second extension product from the first extension product; and

e) hybridizing the first signal primer to the displaced second extension product and extending the hybridized first signal primer on the second extension product such that a double stranded secondary amplification product is generated.